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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/690,454	10/18/2000	Steven M. Ruben	PZ006P1C1	1914

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EXAMINER
CARLSON, KAREN C

ART UNIT	PAPER NUMBER
1653	11

DATE MAILED: 04/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/690,454	Applicant(s) RUBEN ET AL.	
	Examiner Karen Cochrane Carlson, Ph.D.	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11,13 and 17-76* is/are pending in the application.

4a) Of the above claim(s) *1,13 and 17-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11 and 25-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☒ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's election with traverse of Invention II, Claim 11 and new Claims 25-76 in Paper No. #9, filed February 19, 2002 is acknowledged. The traversal is on the ground(s) that it would not be a serous search burden on the examiner if all claims were searched. This is not found persuasive because the claims are drawn to patentably distinct inventions involving different products and/or methods and therefore the search and issues involving the inventions would be lengthy and burdensome.

The requirement is still deemed proper and is therefore made FINAL.

The Examiner acknowledges that the restriction requirement did not take into consideration that each SEQ ID NO:X or SEQ ID NO:Y designates different nucleotide or amino acid sequences. The Examiner appreciates Applicant's limiting the new claims to a single sequence, SEQ ID NO: 59. Noting that Claim 11 was not so limited, A telephone call was made to Janet M. Martineau on April 23, 2002 requesting that Claim 11 be considered as if it were limited to the polypeptide comprising SEQ ID NO: 59, and Ms. Martineau returned the telephone call stating that it was the intention of Applicant to have Claim 11 so limited. See the attached Interview Summary.

Claims 2-10, 12, 14-16 have been canceled. Claims 1, 13, and 17-24 have been withdrawn from further consideration by the Examiner because these Claims are drawn to non-elected Inventions. Claims 11 and 25-76 are currently under examination.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 26-76 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The instant Claims are directed to SEQ ID NO:59, portions and fragments thereof, variants, including those polypeptides having 90% or 95% sequence identity thereto, allelic variants, and species homologs thereof. At page 24 of the specification, the polypeptide encoded by Gene 13, which polypeptide comprises SEQ ID NO: 59, is discussed.

Gene 13 is expressed in keratinocytes, and to a lesser extent in endothelial cells and placenta. Therefore, the detection of the encoded polypeptide is stated to b useful for differential identification of these tissues or cell types. This is not a specific utility because the expression of the gene and detection of the polypeptide would not identify a single tissue or cell type, but all of kerotinocytes, endothelial cells, and placenta. Compare with insulin expression in pancreatic islet cells. The cell type is specific, and therefore if insulin were to be detected in cells one could conclude that the cells were islet cells.

Because the specification concludes that detection of polypeptide can differentially identify tissues and cell types, the identification of diseases and conditions including integumentary or vascular disorders and particularly impaired wound healing and autoimmune disorders can be diagnosed. Keratinocytes and endothelial cells are found throughout the body and do not indicate a disease state. The placenta, of course, is found in pregnant females, and identification of polypeptide in the placenta is not indicative of any disease state. The specification further states that expression of the gene at significantly higher or lower levels may be routinely used in the detection of integumentary, endothelial, and cancer and wound tissues or body fluids for the of a disorder. However, the specification does not teach that the expression of the gene or its encoded polypeptide are expressed at different levels in different disease states in keratinocytes or in endothelial cells, and the function of the polypeptide has not been disclosed, that is, there is no showing that the gene has increased expression in cancerous tissues, for example, or is associated with tissue/cell growth. Expression of a gene and its encoded protein does not indicate its function. Again, compare with insulin expression. The

expression of insulin in pancreatic islet cells does not indicate that the expression of insulin is associated with pancreatic cancer cells, for example.

At page 25, the specification states that the polypeptide is useful for the treatment of wound healing deficiency and skin disorders, including congenital disorders, integumentary tumors, injuries and inflammation of the skin, atherosclerosis, utica, eczema, photosensitivity, autoimmune disorders, keloids, and so forth. It appears that the specification is taking both sides of the issues, that is, that the polypeptide is responsible for tumors and can be used to treat tumors, for example. It is art recognized that if it is true that the polypeptide is responsible for tumor formation, then inhibition of the polypeptide may be useful for treatment of the tumor. The function of the protein is not known, and therefore no conclusion about its usefulness can be made. Therefore, the polypeptide lacks patentable utility.

It appears that the post-filing art disclosing a large potion of SEQ ID NO: 59 is not clear about the function of the polypeptide. Both Feng et al. (2000; Am. J. Pathol. 156(4):1253-1261) and Wiley (2001; WO 01/45730) teach a 129 amino acid sequence that is identical to SEQ ID NO: 59 from amino acid 1 to 106, and sharing 93.9% identity to SEQ ID NO: 59. See the alignments attached to each reference. Feng et al. teaches that FN14 immediate-early response gene encodes a cell surface-localized type Ia transmembrane protein. It is expressed at high levels after FGF treatment in fibroblasts *in vitro*, and is expressed at relatively high levels in heart and kidney *in vivo*. Fn14 is expressed at low levels in normal liver tissues but at high levels during liver regeneration and is highly expressed in hepatocellular carcinomas. Thus, FN14 plays a role in hepatocyte growth control and liver neoplasia. Wiley teaches that this same sequence is a TWEAK receptor, wherein antagonism of this receptor is useful for inhibiting angiogenesis and receptor agonist is useful for promoting angiogenesis. TWEAK is a member of the tumor necrosis family and is expressed in a wide variety of tissues and induces endothelial cell proliferation and angiogenesis. The TWEAK receptor is comprised of a 78 amino acid extracellular domain

(including signal sequence), a 23 amino acid transmembrane domain, and a 28 amino acid intracellular domain. The adult TWEAK receptor is strongly expressed in heart, placenta, and some skeletal muscle samples. The fetal TWEAK receptor expression was ubiquitous and transcripts were seen in the lung and in the liver.

While the exact sequence of SEQ ID NO: 59 (that is, the sequence of Feng et al. and of Wiley et al. differ in the last 6 amino acids of SEQ ID NO: 59 and the sequences of Feng et al. and Wiley are 16 amino acids longer in length) is not taught in either Feng et al. or in Wiley, it is clear that the Fn14 or TWEAK receptor polypeptides are at least 90% identical to SEQ ID NO: 59 and are variants or homologs thereof. In either event, or in all events, the action of Fn14 and of TWEAK receptor has been demonstrated, and these activities do not correspond to those activities surmised for SEQ ID NO:59 of the specification. Therefore, the teachings of Feng et al. and of Wiley support this rejection of the claims, that the specification does not provide a specific or substantial utility for the amino acid sequence SEQ ID NO: 59.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 25-76 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 11 and 37-76 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These Claims set forth variants and fragments of SEQ ID NO: 59. However, no activity is provided for these variants and fragments and therefore one skilled in the art would not know the claimed sequence having 90% identity to SEQ ID NO: 59, for example, because there is no measureable function associated therewith. Therefore, the claimed variants and fragments lack written description because the specification does not teach sequences having 90% identity to SEQ ID NO: 59, for example, and having a specific activity.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 703-308-0034. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low can be reached on 703-308-2329. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Karen Cochrane Carlson

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER